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A PORCINE MODEL FOR VIDEO-ASSISTED THYROIDECTOMY

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A minimally invasive approach for surgery of the thyroid is suitable either for the better esthetic results or for the possibility of a decreased risk of injury to the recurrent laringeal nerve and parathyroid glands due to the magnification of the laparoscope.

Although some differences exist between human and pig's anatomy, a porcine model for endoscopic thyroidectomy is useful for testing the safety of neck insufflation and for teaching this advanced tecnique.We operated six female pigs (Landrace) weighting from 20 to 25 kg. Under general anesthesia a small incision is performed close to the sternal bone, 2 cm on the left of the midline. After the platisma muscle is exposed, dissection is carried out to allow the vision of the sternocleidomastoid muscle; at this point a 10 mm trocar is inserted and insufflation of CO2 is performed up to 12 mmHg. A second trocar (5 mm) is then inserted 2 cm laterally and 4 cm higher with respect to the first trocar. The third trocar is positioned on the same line of the second one, 2 cm below the angle of the jaw. Dissection is continued in the fat and fibrous tissue that connect the sternoioideal and the sternocleidomastoid muscles. In this way the trachea with the sternothyroid muscles can be easily exposed and the two muscles can be separated in the midline in order to allow thyroid exposure. The inferior thyroid peduncle is approached first and its adhesions with the trachea are interrupted. Thus the thyroid is lifted up and the inferior thyroid artery and vein can be sectioned between clips positioned by a 5 mm clip applier on each side of the gland. Afterwards the superior thyroid peduncle is dissected on both sides and the small vessels are coagulated and interruped. The thyroid is than placed in a small bag prepared by performing a tobacco pouch on the free edge of a glove's finger in order to extract it through one of the two 5 mm trocar sites. Using this kind of approach we were able to perform thyroidectomy with a good exposure of the structures of the neck. We did not experience bleeding and subcutaneous emphisema was always limited to the neck. The approach we used seems to allow a very good exposure of the thyroid and to avoid massive subcutaneous emphisema. This animal model can be used to test CO2 neck insufflation effects and to improve surgeons' skill with the minimally invasive tecnique.

AESTHETIC RESULTS AFTER CONSERVATIVE TREATMENT OF BREAST CANCER

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After conservative treatment for breast cancer some not aesthetic sequels may be observed (i.e. asimmetry, deformity).

We evaluated the aesthetic results of 70 patients (average age: 58 yrs) that received a conservative treatment in a series of over 1110 cases operated for breast cancer. Conservative surgery was performed in these patients: in 66 cases (94.3%) a upper-external quadrantectomy, while in the other 4 cases (5.7%) a lower-extern one. Post-operative radiation therapy was administered in all the cases.

14 patients (20%9) had a small breast, 46 (65.8%) had a medium breast, 10 (14.2%) had a big one. 54 patients (77.1%) had a radial incision, 34 (48.5%) had separated axillary and skin incision.

We evaluated, using Van Limberg's score, the upper and the lateral retraction. We also reported the aesthetic judge of a doctor, of the patient and of a nurse in a scale from 0 to 10. They considered: asimmetry, iperpigmentation, teleangectasy and edema of the breast. The patients were shared in different groups as regard to the different degrees of asimmetry and for each of them we compared aesthetic judge, kind of incision (radial or circular, continued or separated) and breast size. We also shared patients regarding to the size of the breast, and we relationed it to the aesthetic judge and to the kinds of asimmetry.

On the basis of the obtained results, we concluded that big postoperative asimmetries are not necesserely related to worst aesthetic results, because those are more common in the biggest breasts, were lack of tissue and scar reaction are less evident and volume compensation is more likely.

MORPHOLOGIC CYTOLOGICAL CLASSIFICATION OF THYROID NODULE - CLINICAL VALUE IN PREOPERATIVE MANAGEMENT

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Fine needle aspiration biopsy (FNAB) of thyroid nodules facilitates the selection of patients for surgery, but the management of follicular nodules (FNs) is still a clinical dilemma and histologic examination is usually required for an exact diagnosis.

We evaluated the reliability of a morphological cytologic classification of FNs for a preoperative assessment and a better selection of the patients for surgery.

We retrospectively analyzed 117 cases with diagnosis of FN and with a histological control, consecutively observed between 1993 and 1997. All the cytological specimens were classified in 3 categories, according to morphological criteria: Thyreocytic Hyperplasia Without Nuclear Atypia (THWNA), Predominantly Follicular Lesion (PFL), Follicular Lesion With Nuclear Pleomorphism (FLWNP).

Among all the cases, 40 (34.2%) were THWNAs, 64 (54.7%) PFLs and 13 (11.1%) FLWNPs. The cytohistological correlation showed a low incidence of neoplasm, either benign or malignant, in the first group (follicular adenoma: 11.9%; carcinoma 0%), a higher rate in the second one (follicular adenoma: 36.3%; carcinoma 7.6 %). The highest rate of adenomas and malignancies was found in the third group (42.9% and 42.9%, respectively). The difference among the three groups was statistically significant, considering both the percentage of neoplasm ($p=0.00003$) and of malignancy ($p=0.08$).

This results suggest that this classification could represent a guide for the management of FNs. A conservative approach is suitable in case of THWNAs, while, because of the risk of malignancy, surgery is advisable in case of PFLs and mandatory in case of FLWNPs.

SURGERY FOR ADRENAL MYELOLIPOMA

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Adrenal myelolipomas are rare (prevalence: 0.08% - 0.2) and less than 300 cases have been reported in the western literature. Incidental diagnosis of myelolipomas, however, is reported with increasing rates (7-15% of all the incidentalomas). They are composed of mature fat cells and hemopoietic elements of bone marrow, in various proportions and a slow growth. Myelolipomas are frequently associated with chronic illness, malignancy and/or endocrine disorders. Sometimes they may be complicated by hemorrhage or retroperitoneal rupture.

We observed 6 patients (5 men and 1 woman) with incidentally diagnosed adrenal myelolipoma. Each of them had a careful laboratory and instrumental evaluation. Two patients complained of vague symptoms of compression; 3 of them were hypertensive; 1 patient, who was affected also by gastric leyomioma, colelithiasis, omolateral renal angiomyolipoma and diabetes mellitus, complained of dyspespia. No biochemical alteration was observed. US and CT had a sensitivity of 80% and 100% respectively. All the myelolipomas were unilateral (4 on the right, 2 on the left side). The lesions size was between 4,5 and 10,5 cm (8,6 cm in average). 5 patients were operated on. 1 asymptomatic patient, the only one in whom FNAB was performed, with cytological diagnosis of myelolipoma, refused surgery. Adrenalectomy was performed in all the operated cases. No postoperative complications was observed.

On the basis of these results and of a review of the literature, we conclude that surgical excision, when possible by laparoscopic approach, is indicated in presence of symptoms and complications and in cases associated with lesions of adrenal gland or other organs

requiring surgery; surgical excision is also indicated in case of suspicion of malignancy and/or large size (> 6 cm). Adrenal gland must be excised *en bloc*, also because of the possible presence of other adrenal lesions.

RECURRENT PHEOCHROMOCYTOMA: A CASE REPORT WITH AMBIGUOUS URINARY CATECHOLAMINES ASSAYS

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Background. Recurrent pheochromocytoma (RPh) is not so rare and it may be a diagnostic challenge when laboratory tools give uncertain results. We report a case successfully treated by reintervention, in which MIBG scan resulted as the only definitive diagnostic tool despite of ambiguous urinary catecholamines (UC) assays.

Methods - Results. The patient was a 33 yrs. old woman submitted to left adrenalectomy for pheo 2 years before; pathology suggested a malignant nature because of capsular invasion. Primary resection was radical, and obtained a complete remission of symptoms (paroxystic hypertension, headache, precordial pain, tachyarythmia). 18 months later, she complained a relapse of cardiac symptoms, without hypertension; UC were normal in repeated assays and a psychiatric evaluation for "anxious state" was suggested. Further evaluations during hospital stay revealed high UC only in 1 of 4 assays; an abdominal CT scan showed a 8 cm mass above the left kidney. MIBG scan confirmed a left suprarenal uptaking lesion suggesting RPh. At reintervention, a multinodular (main node measuring 2 cm) neoplasm, inferomedial to the left kidney, was resected; pathology confirmed a RPh. The postoperative course was uneventful, and the patient is well and symptom-free at 6 months; UC are normal.

Conclusions. In a symptomatic patient previously undergone to surgery for pheo, recurrent disease should not be excluded only on the basis of negative urine tests, and MIBG evaluation is advisable because of its high specificity for these lesions. As in diagnosing pheo for the first time, the risk of a late diagnosis due to minimizing patient's complaints should be avoided.

PROGNOSTIC SIGNIFICANCE OF EXPRESSION OF GEM PROTEIN IN BREAST CANCER

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BACKGROUND - Recently, several biological prognostic markers has been analyzed for breast cancer, but no conclusive results have been obtained. Gem, an induced immediate early protein belonging to the ras family, has been recently suggested to partecipate in receptor-mediated signal transduction at the plasma membrane. We evaluated the expression of Gem in breast cancer and its correlation correlation with the pathological prognostic markers.
METHODS - We analyzed a series of 54 consecutive patients treated for breast cancer at the Department of Surgery of the Catholic School of Medicine in Rome. On the surgical specimens, the cytoplasmatic concentration of Gem was measured by an immunoistochemical assay. We utilized the avidin-biotin peroxidase complex method with a policlonal antibody anti-Gem. The concentration of Gem was compared to the standard prognostic factors for the disease and related to disease free and overall survival: a statistical analysis was carried out.
RESULTS - Gem expression was significantly related to histological subtype and more frequently present in infiltrating ductal carcinoma (p=0.04). A statistical correlation was also found beetween gem expression and lymphnodal status: Gem expression is more frequent in N+ cases (p=0.04) and in the patients with more than 3 lymphnodes invaded (p=0.004). No other statistical significant correlation was found between the investigated maker and the standard prognostic factors and between Gem protein and the overall and disease free survival.
CONCLUSIONS - Although data are limited and not conclusive, the expression of Gem protein is related to a more aggressive lesions. Anyway, further and more extensive evaluations are necessary in order to verify the clinical reliability of this biologic marker as prognostic factors in breast cancer.

DOCETAXEL AS SALVAGE CHEMOTHERAPY IN ANTHRA-CYCLINE-RESISTANT BREAST CANCER PATIENTS (pts)

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Docetaxel (TXT) has demonstrated high activity as single agent in metastatic breast cancer, showing in non-pretreated pts 37-87% and in previously treated pts 34-60% of objective responses, and, moreover, TXT is highly effective in anthracyclines resistant disease (up to 56% of responses). From October 1996, 22 metastatic breast cancer pts were treated with TXT (100 mg/M2 i.V. over 1 hour infusion d 1 q 3 weeks).Pts characteristics were: median age (range) 55.5 (31-76), median VHO PS (range) 0 (0-3), pre/postmenopausal 9/13, prior adjuvant chemo-hormonotherapy 12/5, prior anthracyclines for metastatic disease 20/22 (two out of twentytwo pts had been treated with anthracyclines-containing adjuvant regimen with disease free survival < 12 months), dominant disease sites were: soft tissue 1, bone 2, viscera 19 pts (liver metastases, 16 pts), number of metastatic sites: 1 in 4, 2 in 10, 3 in 8 pts. In 18 evaluable pts (4 too early) we observed: 1 RC (5.5 %), 5 PR (27.5%), for an overall response rate of 33%.Median time to response was 3 months (range 2-8 months); the median number of treatment cycles was 3 (range 1-8). All the pts with visceral involvement achieved an objeetive response (2 CR on liver metastases).Myelosuppression was the dose-limiting toxicity, with G3-G4 neutropenia in 64% of the pts; neutropenic fever was observed only in 14% of the pts; G-CSF 300 ptg/day subcutancously from d 6 to 17, was given in case of G4 neutropenia (50% of the pts). Nonhematologic toxicity was generally mild, with nausea and vomiting occurring in 13% of the pts; mucositis, diarrhea, asthenia, in 9% of the pts; peripheral neurophathy in 9% of the pts; arthralgias in 4% of the pts. Neither hypersensitivity reactions nor severe fluid retention were recorded.In conclusion TXT appears to be an active drug against anthracyclines-resistant metastatic breast cancer, with moderate toxicity and high efficacy on visceral metastases but the use of prophylactic growth factors is required.

Uncommon metastases of breast cancer

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Breast cancer may present with a wide multiplicity of distant metastases. Two rare cases of metastases, one to the thyroid gland and one to the buttock from a subclincal breast cancer, are reported. A 72 years old woman, opcrated 5 years before of mastectomy for locally advanced infiltrating ductal breast cancer and affected from squamous cell carcinoma of the lung, was admitted for severe pressure and choking symptoms due to a big nontoxic goitre of the right lobe Submitted to hemythiroidectomy the histological examination revealed that the enlargement of the thyroid gland consisted of a metastasis of breast cancer with positive estrogen and progesterone receptors. Even if mietastatic disease to the thyroid gland is not as rare as previously considered it is usually a diagnostic dilemma. Our observation confirms that in any patient with a previous history of carcinoma, a thyroid mass should be regarded as a metastatic malignancy until proved otherwise. Although metastasis to the thyroid gland occurs often simultaneously with other metastases and indicates poor or terniinal prognosis, aggressive surgery may be mandatory because of pressure syinptoms.A 84 years old wonian presented with a subcutaneous mass, 10 cm big in greatest dimension sited in one buttock. The removed mass histologically turned out to be a carcinoma compatible with metastasis of medullary breast caiicer. Neither breast symptoms, nor demonstrable metastases to regional lymph nodes were present. Mammography showed a non palpable breast density strongly suggestive of malignancy. It was decided to avoid unnecessary diagnostic procedures and hospitaliazation. Tamoxifen was prescribed.
The case is an example of the great heterogeneity of the clinical presentation of metastatic malignancy of the breast.

Adjuvant treatment of high risk resectable breast cancer: high dose chemotherapy with peripheral stem cell transplantation.

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Breast cancer is the most frequent female cause of mortality due to cancer in Western countries. Among the pts with breast cancer which according to the diagnosis could be operated in 60% of cases the lymphonodes are metastatic and the 50% of these presents more than 3 positive lymphonodes, particulary the 25% from 4 to 9 and the 20% 10 or more. The prognosis in pts with more than 3 metastatic lymphonodes gets worst and in particular those pts with more than 10 positive lymphonodes have a probability of relapse which goes respectively from the 55 to 85% within 5 years and from 70 to 90% within 10 years, indipendently from the receptorial status and chemotherapy effected. It is recognized how for some chemotherapeutic drugs (and in particular for the Alkylant agents: Cyclophosphamide, Cisplatin, Melphalan) the dose response curve shows a particularly rapid advancement. At present by meance of hemopoietic support rappresented by peripheral blood stem cells (PBSC), supported also by growth factors employment the effects of myelodepression can be reduced. It is for such reason that we have started with a study on high dose chemotherapy with PBSC transplantation in pts with resectable breast cancer. 15 pts are enrolled with these eligibility criteria: histologically confirmed breast cancer with 4-9 lymphonodes involved, G3, ER-, or with 10 or more positive lymphonodes, undergone to surgical treatment within 6 weeks, without distant metastases, age between 18-60 years, renal cardiac, pulmonar, hepatic and neurological functionality as well as normal hematochemical parameters. Our therapeutic program includes a first cycle of *induction* chemotherapy with: 5FU= 500 mg/m^2, d.1; EPI=90 mg/m^2, d.1; CTX 1500 mg/m^2 d.1 + G-CSF=300 µg/d. s.c. from d.3 for 8-10 days till the apheresis, for recruitment of PBSC. Further three cycles of chemotherapy are administrated every 21 days according to the following schedule: 5FU= 500 mg/m^2, EPI=90 mg/m^2, CTX 600 mg/m^2 supported by growth factors on alternate days if hematological toxicity arises. Thereafter pts undergo to 1 cycle of intensification according to the following schedule: Carboplatin= 600 mg/m^2 days -4,-3; Etoposide= 450 mg/m^2 days -4,-3; Melphalan= 50 mg/m^2 days -2,-1; PBSC reinfusion day 0. The patient is isolated in a laminar-flux room up to complete recovery of hematologic parameters. Hematologic toxicity of 4 grade (WHO) has been founded out with a rapid hemopoietic recovery. Extrahematological toxicity is moderate in all but one pt who has shown mycotic sepsis treated with Amphotericine B. At present only two pts have relapsed, while the other 13 pts are alive and disease-free with a median follow-up time of 14.5 (range 7-60 months).

BREAST NON-EPITHELIAL NEOPLASMS

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Breast epithelial glandular neoplasms alone account for 95% of malignant breast cancers; the remaining 5% concern mixed glandular tumours and other tumors involving extragiandular tissues. Among these rarities, a privileged place is occupied by breast linfomas, soft tissue cancers, and phylloide cancer. These neoplasms - that sometimes appear as different pathologies or breast benign pathologies have in common a tricky clinical presentation, the lack of pathognomonic instrumental reports, as well as uncodified medical and surgical therapies. In the wake of some cases of mixed glandular tumours and breast extraglandular cancers observed at Surgical Pathology Division in 1997, and while underlying the diagnostic and therapeutic difficulties encountered, the Authors analize the problems of these rare neoplasms, comparing the experience reported in Literature. They propose a more cautious therapeutic approach and recommend the planning of a multicentric study aiming at obtaining greater clarity on the trend of these breast neoplasms, whose prognosis is also different from that of more common epithelial breast neoplasms.

Breast Cancer in young women (35 or less); biological and prognostic features.

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From 1984 to 1994, 2475 women were observed with breast cancer; 64 were aged 35 or less (2.4%).No pregnancy and family history were 37% and 32.2%.In the older group respectively were 19.2% and 15.5%. Diagnosis was casual on 75% of the young women. TI NO was found only on 14.5%. T2 T3 N+ was on 85.5%.ER status was positive only on 25.7%; in the older group the same was 75%; the difference was significant, but expected.G3 was found on 45.1%. Nodes involvment was 63%; the older group had 22.3%. Mastectomy was performed on 77.4%, 66.1% had a adjuvant chemotherapy (CHT); 11.6% had hormonotherapy; for 3.2% both; 29% had no treatment. Analysing the stage: the early had a O.S. of 85% unchanged until 12 years. The D.F.S. after 5 years was 71.4%; the some remains until 12 years.The advanced stage had a O.S. respectively of 58.3% (5 years), 42.2% (10 years), 31.7% (15 years); the DFS was 33.5%, 30%, 15% respectively.In the older group the DFS was 80% after 5 years, 25.1% after 10 years. The data show the precocity of the disease is function of the biological and prognostic features.

TOTAL AXILLARY LYMPHECTOMY IN T1N0M0 BREAST CANCERS. A MATTER FOR DEBAT'E

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From May 1987 trough December 1996, 362 patients have been admitted in our centre due to a breast malignancy.Ninety-five of them presented without clinical palpable lymphonodes.The treatment of choice in these patients has been a wide local excision (quadrantectomy, 53 pts) followed by a I-II. level lymphectomy and subsequently by local radiotherapy.(QUART protocol). In the remaining 42 pts a classic Madden's modified radical mastectomy was performed. Also these 42 pts underwent a I-II level lymphectomy.Two of these patients died 36 months after the first surgical treatment, one- due to a local recurrence associated with lung metastases and the other one after developing a second breast malignancy.Three patients had a local illness recurrence. Fifty-two have been followed at least for five years.
According to our experience and to the recent literature we conclude that a two level (I-II) axillary lymphectomy may be considerd a rational treatment during procedures for T1N0M0 breast cancers.

Tubular carcinoma of the breast: analysis of 8 cases

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Tubular carcinoma of the breast is a rare, well-differentiated histological subtype of invasive carcinoma. Review of the literature reveals a frequency of 0.7-1.5% of total cases of invasive breast carcinoma with favourable prognosis. (5-year relative survival over 90%).
From 1988 to 1995 eight cases of tubular carcinoma were diagnosed. The mean age was 60 years (range, 35-82). Three cases were premenopausal women. Four patients underwent modified radical mastectomy, and four segmental mastectomy (3 quadrant excisions, 1 lumpectomy without axillary dissection for a 0.5 cm size tumour). The mean pathologic tumour size was 1.4 cm (range, 0.5-2). No multifocality was observed. The mean number of lymph nodes, in seven axillary specimens, was 18 (range, 10-25). In one patient, there was lymph node metastasis to a single node (12.5% incidence). All the patients are alive, with a mean follow-up of 5 years (range, 2-9 years). One of them (stage pT 1 c, NO) is under treatment with tamoxifen for a local skin recurrency occurred 6 years after radical mastectomy performed in postmenopausal age. Our analysis confirms the low frequency of this variant of infiltrating ductal carcinoma and its favourable prognosis also when treated with breast preservation surgery. Nevertheless our experience substantiates that lymph node metastases though rare can occur and, for this reason, axillary dissection should always be perfomed.

MULTINODULAR GOITER, AN INVOLVING THE WHOLE GLAND DISEASE

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Subclinical deficiency of thyroid hormone production, increased secretion of TSH and consequent diffuse hyperplasia with proliferation of different clones of thyrocytes are the most accepted theories in the pathogenesis of multinodular goiter. This model has been partly revised: several growth factors, particularly IGF-1, are supposed to induce thyrocyte maturation and mitosis. Some of these factors are produced "in situ" by selected clones of thyrocytes. These clones seems to be present also in areas which did not apear to be macroscopically involved by the hyperplastic process, suggesting a possible wider involvment of the gland.Samples were obtained since January 1995 from 20 thyroid after total thyroidectomy for nodular goiter in which almost 1 lobe in each gland was characterized by normal volume and no apparent nodular lesions. Every gland was sectioned at 1 cm intervals in both lobes; 3 sections from each isthmus were obtained, too. In order to obtain sections representing the whole gland, from every sample 1 slide after fixation and staining for histopatological evaluation was randomly choosed. Totally 1020 slides were obtained; 660 resulted from areas macroscopically involved by hyperplastic process, 360 from apparently undamaged areas. 740 slides were characterized by an extension of the hyperplastic lesions wider than 75% of each microscopic sample (pattern type A); in 270 the extension resulted less wide than 75% (type B). No lesions were observed in 10 slides (type C). Samples from areas macroscopically involved were in 59% characterized by a pattern type A, in 41% type B and 0% type C. In areas without any apparent hyperplastic disease 2.5% slides werte classified in type A; 94.2% in type B and 3.3% in type C. These data suggest that morfological features characteristic of multinodular goiter are detectable in areas macrscopically or clinically not involved by the hyperplastic process. Multinodular goiter is indeed a disease which globally involves the thyroid gland, even when it shows clinical or macroscopically signs of partial involvement. It could be characterized by focal lesions with multistep evolution or a diffuse disease with partial expression at early stages. The histopatological evidence is that the initial stage of hyperplastic proliferation do not have nodular appearence; it seems to start with a macroscopically inapparent, circumscribed but not demarcated growth of follicles. lesions, would suggest total thyroidectomy as the treatment of choise for this disease.

Vinorelbine (VNB) and Paclitaxel (P) simultaneously infused in previously untreated advanced breast cancer (ABC) patients (pts)

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The synergistic antitumor effect of the simultaneous administration of VNB and P in preclinical models of breast cancer cell lines, induced us to carry out a study to evaluate activity and toxicity of this association as first-line chemotherapy in ABC pts. Based on a previous phase I study by N. Ibrahim, in which MTD was 25mg/M2 and 150 mg/M2 P simultaneously administered by 3-hr infusion every 3 weeks, we used the same dose and schedule with G-CSF support. As we did not observe severe hematologic toxicity in the first 10 pts treated, G-CSF was subsequently omitted. Thirtythree pts with ABC entered the study. Their characteristics were the following: median age 53 years (29-71), median VMO Perfomance Status 1 (0-3), pre/postmenopausal 8/25, prior adjuvant chemotherapy 16 pts (8 CMF, 8 anthracyclines-based chemotherapy). The dominant disease sites were soft tissues, bone, and visceral, respectively in 6, in 7 and in 20 pts.. Thirty-one pts were evaluable for response (lost to follow-up: 1; treatment interrupted for G4 epatotoxicity at first cycle: 1).Objective responses were observed in 15 pts, for an overall response rate of 48% (95% CI, 31-65%). They include 1 CR (3%) and 14 PR (45%).Median time to response was 2 months (2-7), median duration of response and median time to progression 7 months. Median survival has not been reached. Median number of cycles administered was 6 (1-6). Responses according to dominant site of disease were 50% in soft tissue and in bone,and 47% in visceral sites. The treatment was well-tolerated: the DLT was neutropenia (G3-4 in 44% of the pts); there were only 2 cases of neutro penic fever. Other toxicitics were universal alopecia, GI/2 emesis and transient peripheral neurotoxicity in 47% of the pts.

Conclusions.- The activity of VNB and P as first line-chemotherapy in ABC is only moderate at the dose and schedule used in this study. The mild toxlcity of the treatment let us suppose that better results could come from higher doses of the drugs with G-CSF support.

CEF + G-CSF AS PRIMARY CHIEMOTHERAPY (PCT) IN LOCALLY ADVANCED BREAST CARCINOMA

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Fiftythree patients (pts) with histologically proven locally advanced breast carcinoma (T4 and/or N2), were allocated to receive PTC with the aim to evaluate the percentage of tumors rendered fully operable by PCT, and to improve disease free survival (DFS) and overall survival (OS). Pretreatment evaluation included: history and physical evaluation, with bidimensional tumor measurements, automated blood cell count, biochemical profile, chest x ray, ECG, radionuclide angiography (MUGA SCAN), liver ultrasound, bone scan, bilateral mammography and breast ultrasound, 99 mTc-MIBI breast scintigraphy (MIBI), and a small (1 cm) incisional biopsy of primary lesion to determine the histologic findings and some biologic parameters (glicoprotein p-170 expression, hormonal receptors status, HER 2/neu, PCNA, p-53, bcl-2).Characteristics of the pts: median age 55 years (range 30-60), pre/post rnenopausal 18/35, ER+/ER- 31/22, T >5 cm 6, T4 38, T438, medium initial T diameter 7 cm, clinical N+/N- 74%/21%.The regimen administered was CEF (Cyclophosphamide 400 Mg/n,2, Epirubicin 50 fflg/M2 , Fluorouracil 50 Mg/M2) i.v. on d 1 and 8 q 3 weeks for three cycles, + G-CSF 300 µg subcutaneously every other day from d 5 to 17. After a fully revaluation, whenever possibile (favourable ratio residual tumor/breast) a quadrantectomy plus axillary dissection was performed; otherwise a Patey radical mastectomy was performed.Subsequently, responder pts received the same regimen as adjuvant chemotherapy (3 cycles), while non-responder pts received a non cross-resistant chemotherapy (vinorelbine 25 mg/M2 d1,8, plus mitomycin C 1 0 mg/M2 d 1, every 4 weeks for 3 cycles). In case of conservative surgery or initial T4d, radiation therapy was performed at the end of adjuvant treatment.

Moreover, ER+ pts received Tam 20 mg/d for 5 years. In 50 evaluable pts (3 too early) we observed: 1 CR (2%) and 38 PR (76%) for an overall response rate of 78% (95% CI, 66.5-89.5%). No pts showed tumor progression while on PCT, and all the tumors were rendered fully "operable" by primary CEF. There were performed 9 (18%) quadrantectomy and 41 (82%) radical mastectomy. Myelosuppression was the most important side effect, with G3-G4 neutropenia in 63% of the patients; the planned dose-intensity was maintained in 74% of the pts. We did not observe clinical or laboratory cardiotoxicity. With a median follow up of 28 months, distant recurrences were observed in 22 of the pts (41.5%). No local recurrences post conservative surgery were recorded. The 3-year DFS and OS were 52% and 71%, respectively. Correlations among various prognostic factors and recurrences were the following: pre/post rnenopausal: 55%/37.5%; ER+/ER-: 42%/41%; T > 5 cm: 67%, T4: 34%,T4d: 55%; PN+: 51.5%, pN-: 29%; responders: 49%, non-responders: 27%.Our data show a high rate of objective response to primary CEF, with and excellent local control and some chances of breast preservation, and an increase in 3-year DFS and OS but, contrarily to some literature data, we did not find a correlation between the response to PCT and pts outcome, or among other prognostic factors and DFS. The only important prognostic factor in our study was the axillary nodal involvement, while the administration of a non-cross resistant adjuvant regimen to non responder pts could presumely improve DFS of the pts.

THE RELAPSE FOLLOWING LOBECTOMY DUE TO MONOLATERAL BENIGN NODULAR PATHOLOGY: ELEMENTS OF ASSOCIATION AND THERAPEUTICAL PROBLEMS.

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INTRODUCTION

When the pre-operative scan and intra-operative assessment reveal the presence of unilobar multiple or single nodules, while the controlateral side seems to be completely spared, conservative surgery is advised. During follow-up period may be observed a recurrence, after short-term too.

OBJECTIVES

The purpose of our work is to assess if monolateral multinodularity is associated with the post-operative recurrence.

METHODS

We examined 109 patients, followed at our center, who undergone lobectomy+istmectomy surgery, due to benign pathology of a single thyroid lobe. Follow-up period lasted up to 3 years at least. The patients were divided into two groups, according to their clinical pre-operative condition: group A - patients with a single nodule (n.51), group B - patients with monolateral multinodular goiter (n.58). We also considered the therapeutical protocol established after surgery: 1) patients treated with suppressive dosages of L-tiroxine (n.35), 2) patients treated with non-suppressive dosage of L-tiroxine or patients not in therapy (n.74).

RESULTS
A total of 51 relapses were observed, equal to 47% of controls. In group A, the recurrence rate was significantly lower than group B patients (33% and 58% respectively, $p<0.01$). Post-operative hormonal therapy results did not reveal significant differences in the two study groups (relapse rate of 40% and 46% in patients treated with opotherapy and patients not in therapy, respectively).
CONCLUSIONS
Our analysis shows that the unilobar multinodular pathology has a high recurrence risk, in a short-term as well, which is significantly higher than the uninodular pathology. These data have not been sex and age adjusted. No significant differences were found between the two groups of patients treated with thyroid hormonal therapy as in light of the difficulties encountered in documenting an adequate suppressive therapy promptly initiated post-operatively and administered throughout the period of observation. Since medical treatment may arise several complications (osteoporosis, iatrogenous thyrotoxicosis), radical surgery (total thyroidectomy) in the unilobar multinodular pathology could be advisable only in the absence of post-operative complications, such as hypoparathyroidism or recurrent nerve lesion.

POSITIVE PREDICTIVE VALUE OF MAMMOGRAPHIC SIGNS: A REVIEW OF 181 NON PALPABLE BREAST LESIONS

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PURPOSE
Because of the difficult definition of "patterns of signs" which may also vary among centers it is suitable to always refer to the personal historical Archives (back experience) to verify the personal results.
MATERIALS AND METHODS
181 surgical biopsies of nonpalpable breast lesions (161 from 1988 to 1996) e 20 (by september 1997) were performed following image-guided (stereotactic or sonographic) localizzation. The mammographic findings of these lesions were correlated with histology, age, staging of malignant lesions, positive predictive value (PPV) of radiologic findings, patients' survival and trend of operators' performance over the years according to two procedures. The first concerned the collection of information per year; in the second the B/M ratio per year, biennial and overall in the whole series, was reappraised.
RESULTS and CONCLUSIONS
94 of the excised lesions were malignant and 87 were benign with a 0,92:1 benign-to-malign ratio; 0,52% PPV for malignancy. 19% were in situ carcinomas.
Base on the assessment of data of considered patterns of signs, our results led us to select the following approach:
Systematic excision of all spicular lesions (PPV=83,8%), highly suspicious microcalcifications (PPV=63,8%), opacities with more or less dysmorphic calcifications (PPV=46,6%).
While in literature a less than 1:1 B/M ratio is considered optimal and in our series the attained performance
('88-'89= 2,1; '90-'91= 1,04; '92-'93= 0,57; '94-'95= 0,68; '96-'97=0,82) is satisfactory, a great deal of caution and criticism is necessary in the analysis of these results a further decrease in this B/M ratio means the "loss" of those cases where the "specificity" is of difficult attainement even with a good pratical experience which tends to characterize as normative what by nature is changing and often with no boundaries benignancy and malignancy.

BENIGNANT AND MALIGNANT THYROID DISEASE: CONSIDERATION ABOUT RECURRENT LARYNGEAL NERVES AND PARATHYROID GLANDS VISUALIZATION AND CORRELATED COMPLICATIONS.

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INTRODUCTION. At the present total thyroidectomy (T.T.) is becoming more and more necessary in thyroid surgery. Therefore the visualization and preservation of the recurrent laryngeal nerves (R.L.N.) and parathyroids glands is mandatory.

The aim of the study is to value the anatomical relations of these structures and the complications subsequent to their damage.

METHODS. Thyroid surgery was performed in 329 patients: 253 cases (76.9%) for benignant disease (228 euthyroid pts. = 90.1%; 25 hyperthyroid pts. = 9.9%) and 76 cases (23.1%) for malignant disease.

The operation for benignant disease was rapresented by 186 T.T., 24 totalizations (Tot.), and 43 lobectomy (Lob.); for malignant pathology it was 52 T.T., 19 Tot., and 5 Lob.

RESULTS. Recurrent laryngeal nerves were always visualized. Their relation with the inferior thyroid artery (I.T.A.) was the sequent: on the right side the nerve ran anteriorly in 29.3% of cases, posteriorly in 38.3%, between the branches in 30.0%, the I.T.A. was absent in 1.6% of cases, the R.L.N. was nonrecurrent in 0.8% of cases; on the left side the rates were 23.3%, 49.4%, 24.1%, 3.2%, and 0% respectively.

The parathyroid glands were visualized in 91.7% of lobectomies and in 93.1% of T.T. for benignant disease; for malignant disease the rates were 100% and of the 91.8% respectively. The parathyroid gland more frequently visualized was the right superior one (71.2%), then the left superior (70.3%), the right inferior (42.3%) and at last the left inferior (32.9%).

The complications after R.L.N. lesion caused a transitory deficit in 2% of cases of benignant disease and in 2.6% of malignant disease; in no case a definitive deficit was observed.

Hypoparathyroidism was transitory in 8.6% of cases of benignant disease and in 23.9% of malignant disease; it was definitive in 3.3% and in 2.8% of cases respectively.

CONCLUSION. The recurrent laryngeal nerves were visualized in 100% of cases. More careful dissection is needed when the nerve runs between the branches of the inferior thyroid artery or it is nonrecurrent and when the artery is absent. In our experience no definitive lesion of the nerve was observed.

Hypoparathyroidism is still a fearful complication especially when thyroid surgery is performed for benignant disease. Overall the glands were visualized in more than 90% of cases and the superior ones were the most frequently detected. This permitted to reduce the frequency of definitive hypoparathyroidism to a rate as low as about 3% overall.

RADIOIODINE TREATMENT OF HYPERTHYROIDISM: ITS THERAPEUTIC EFFECT IS EVIDENT BETWEEN THE SECOND AND THE FOURTH MONTH AFTER DOSE ADMINISTRATION.

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Radioiodine (^{131}I) is one of the therapeutic options for hyperfunctioning thyroid diseases. It is safe, effective and almost certainly the cheapest form of treatment of hyperthyroidism. A lot of factors (patient age and sex, thyrotoxicosis degree, administered dose, preteatment thionamides therapy) and the inherent delay in achieving ^{131}I therapeutic effect influence the timing and the pattern of the response to ^{131}I: that's why patients who underwent radioiodine therapy need to be closely followed-up, expecially during the time that immediately follows the dose administration.
We appointed a new follow-up protocol and we used it to prospectively evaluate 33 hyperthyroid patients (28 females, 5 males; 14 Graves' disease, 12 toxic multinodular goiters, 7 autonomously functioning solitary nodules) who underwent radioiodine therapy between October 1990 and March 1996. For the first six months after the therapeutic dose of radioidine, every patient was asked to make a monthly evaluation of serum FT3 FT4 and TSH, taking care of withdrawing thionamides (if they were taking them) only during the three days preceding blood sampling. Accordingly to monthly results, pharmacological therapy was modified or withdrawn. On the sixth month, every patient had a clinical examination, and after that the frequency of subsequent laboratory and clinical cecks was personalized.
By using this protocol, we confirmed the efficacy of ^{131}I therapy in hyperthyroidism (77,7% cases were cured) and we demontrated that persistent hypothyroidism and euthyroidism (our therapeutic goals) mainly establish between the second and the fourth month after dose administration.
We conclude that the first months are the most important in the definition of positive therapy outcome and that our follow-up protocol is very useful: in fact, it allows to early detect patients who need to start substitutive therapy, to withdraw thionamides or to take a second ^{131}I dose, so avoiding the risk of severe hypothyroidism or persistent thyrotoxicosis.

SURGICAL TREATMENT OF HYPERTHYROIDISM

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The most important problems of hyperthyrodism surgery are: the correct indication for the operation, the choice of the right moment for surgery and the extension of the resection.

The authors' experience includes 227 patients with hyperthyroidism who underwent surgery from November 1987 to December 1997: 43 had Graves' disease (8 males, 35 females; average age 38,4 - range 19-54); 87 had hyperfunctioning multinodular goiter (16 males; 71 females; average age 51,4 - range 25-72) and 97 had monolateral autonomous nodules (17 males, 80 females; average age 48,4 - range 25-79). In the first and in the second group patients had total extracapsular thyroidectomy while in the third group lobectomy plus istmectomy was performed.

Each patient was operated by the same surgeon. The operative technique required the identification of the inferior laryngeal nerves from the mediastinum to the laryngeal entrance and preservation of parathyroid glands.

In 29 patients (12,77%; 6 males, 23 females) association with cancer was observed: a neoplasm occurred in 5 cases of Graves' disease (11,62%), in 15 cases of toxic nodular goiter (17,24%) and in 9 cases of hyperfunctioning adenomas (9,27%). There were no deaths and no wound infections. Operative specific complications include: permanent hypocalcemia in 2 cases (0,88%); transient hypocalcemia in 33 cases (14,53%); transient inferior laryngeal nerve paralysis in 3 cases (1,32%). No permanent inferior laryngeal nerve paralysis was observed.

Hyperfunctioning multinodular goiters and monolateral autonomous nodules have preferential indications for surgery. This is a feasible therapeutic alternative for selected patients with Graves' disease but it remains the treatment of choice in case of recurrence of hyperthyroidism after the withdrawal of properly managed medical therapy, and in presence of cold nodules, for the high incidence of carcinoma. The trend to perform total thyroidectomy in Graves' disease and in hyperfunctioning multinodular goiters is that subtotal resection nevertheless may achieve postoperative euthyroidism in conjunction with acceptable risks of recurrence and it is the same rate of specific complications.

Our experience suggests that surgical treatment is a safe and effective procedure in hyperthyroidism if based on a correct indication and if performed with an adequate technique.

Multifocal papillary thyroid carcinoma incidentally discovered in surgery of parathyroid adenoma

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The coexistence of thyroid carcinoma and parathyroid adenoma has been reported since 1956. Although some authors hypothesised an etiopathogenetic relationship between these two pathologies, more recent evidences suggest that the presence of thyroid and parathyroid tumors in the same patient is incidental. This coexistence can be due to the slow evolution of a preexisting asymptomatic thyroid carcinoma and to the increased attention for thyroid gland in patients with hyperparathyroidism.
We report the case of a 66 yr.old female patient with a hyperparathyroidism caused by a basal right parathyoid adenoma localised by ^{99m}SestaMibi + ^{99m}Tc scintigraphy. A multifocal papillary thyroid carcinoma was discovered during surgical procedures for the parathyroidectomy. The patient then underwent a total thyroidectomy, in addition to the parathyroidectomy. The w.b. scintigraphy performed three months after surgery failed to show any residual thyroid tissue. An association between primary hyperparathyroidism and well differentiated nonmedullary thyroid carcinoma has been frequently reported. Our case confirm the clinical relevance of this association. We suggest to routinely evaluate the thyroid gland in all case which underwent parathyroidectomy.

HYPERAMYLASEMIA AS FIRST SYMPTOM OF PRIMARY HYPERPARATHYROIDISM.

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Symptoms of primary hyperparathyroidism are variable, such as nephrolithiasis, peptic ulcer, weakness, fatigability, depression and pancreatic alteration. We present two cases of primary hyperparathyroidism, in which the diagnosis was performed because of the elevated pancreatic enzymes.

Case n°1: A 32 yrs-old female was admitted with epigastric pain irradiated to the left and right hypochondrium, brash and vomiting since one week. The patient complained of weakness, drowsiness, polyuria and polydipsia since four months. At admission laboratory examinations revealed very elevated serum amylase: 1795 UI/l (50-200), severe hypercalcaemia: 24 mg/dl (8.5-10,5), hypophosphataemia: 1,8 (2,5-4,5), elevated urinary calcium: 1116 mg/24 hrs (75-200) and normal urinary phosphorus: 651 mg/24 hrs (220-740), mild renal failure and neutrophilia. Pancreatic ultrasonography documented a slightly enlarged pancreas with a regular structure. The case was complicated by severe bradycardia (pulse rate: 40 bpm), and so a pace-maker was temporarily implanted. At the beginning, the treatment of patient was somatostatin, bisphosphonates, steroids, diuretics, calcitonin and reidratation.
Primary hyperparathyroidism was considered: serum PTH-intact level was 3700 pg/ml (20-90), the neck ultrasonography and the parathyroid ^{99m}Tc - ^{201}Tl scintigraphy documented a right- inferior parathyroid adenoma.
Case n°2: A 66 yrs-old female was referred to us presenting epigastric pain since two months. At the admission laboratory examinations revealed slightly elevated serum amylase: 371 UI/l (50-200) and lipase: 585 UI/l (<190), hypercalcaemia: 12 mg/dl (8.5-10,5), and hypophosphataemia: 1,5 mg/dl (2,5-4,5) with normal urinary calcium and phosphorus excretion.
Primary hyperparathyroidism was considered: serum PTH-intact level was 273 pg/ml (20-90), the neck ultrasonography and the parathyroid ^{99m} SestaMibi + ^{99m} Tc scintigraphy documented a right parathyroid adenoma.
A multiple endocrine neoplasia (MEN) has been excluded in both patients, and they were referred to the surgeon after normalization of calcium serum levels and resolution of abdominal symptoms.
The relationship between hyperparathyroidism and pancreatitis has been reported since the 1960's with a progressively decreased rate, probably because of an early detection and treatment of the hyperparathyroidism.
There are conflicting reports about this relationship but recent studies suggest that hypercalcaemia induces pancreatic injury via a secretory block, accumulation of secretory proteins, and possibly activation of proteases.
The knowledge of this association allows an earlier diagnosis of the hyperparathyroidism, thus leading an adequated treatment of both diseases.

THYROID CANCER IN HYPERTHYROID PATIENTS TREATED BY SURGERY

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The aim of the present study was to assess the clinical relevance of the association between thyroid cancer and hyperthyroidism by retrospectively analysing a series of hyperthyroid patients submitted to surgery. Surgical procedure consisted in sub-total or near-total thyroidectomy for treatment of toxic diffuse and multinodular goitres and lobectomy, alone or associated with isthmusectomy, for toxic adenoma except in those cases with clinical or sonographical detectable nodular lesions in the controlateral lobe considered pathologic during surgery.
Two-hundred-two patients submitted to surgery for hyperthyroidism during the last 20 years were investigated. Patients, 54 male (26.7 per cent) and 148 female (73.2 per cent) were aged between 22 and 88 years (mean: 53.5± 16 years). None had a history of external radiation. ^{131}I scan and sonographic evaluation of thyroid gland was carried in all patients prior to surgery. Thyroid function was assessed by measuring plasma TT3, TT4 and TSH. Methimazole treatment and administration of Lugol's solution for 5 days before surgery were employed to obtain a euthyroid state. After surgery, histologic specimens were re-examined according to the standard approach described by Rosai (1). The mean follow-up in this series was 76 months (range 6-228 months).
Thyroid cancer was diagnosed in 12 cases (5.9 per cent), histological examinations revealing papillary carcinoma in 9 cases, follicular carcinoma in one and Hürthle cell carcinoma in 2 cases. Concurrence of hyperthyroidism and thyroid cancer was more frequent in those patients treated for toxic adenomas (19.5 per cent) than in those with toxic diffuse (5.3 per cent) or multinodular goitres (1.6 per cent). In 8 patients the carcinomatous lesion showed a maximum diameter of lower than 1 cm but, in 5 of these cases unfavourable histologic features, such as local invasiveness and multifocality, were present. Six-228 months after surgical treatment all 12 patients with thyroid cancer are alive and apparently free of residual disease.
It is concluded that hyperthyroid patients, particularly those with toxic adenomas, should be carefully evaluated to exclude the presence of an associated malignancy. Special attention should be focused on the presence of those "occult" lesions to showing unfavourable histologic features.
1. Rosai J. Manual of surgical pathology gross room procedures. Minneapolis, University of Minnesota Press, 1981, pp 13-21.

THYROID CARCINOMA IN AN ACROMEGALIC PATIENT

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Acromegaly is a rare disorder caused by a pituitary GH-secreting adenoma resulting in clinical features caused by the action of GH secreted in excess and mediated in part by IGF-1 (insulin-like growth factor I).
Patients with acromegaly have a 2.45-fold increased rate of malignancy compared to normal subjects: the most frequent are the colon-rectal, breast and renal carcinomas. Data from literature confirm that goiter is very common in subjects with acromegaly: thyroid enlargement occurs in 92% of patients and nodular goiter in about 73%.
This association could be due to the elevated GH-induced IGF-1 serum levels and its direct mitogenic action on specific receptors of the thyroid cells. Other authors demonstrated that IGF-1 does not independently stimulate thyroid growth, but promotes thyroid cell proliferation by potentiating the mitogenic action of TSH.
The association between thyroid carcinoma and acromegaly has been less frequently described.
We report a case of a 27 yr-old female patient suffering from a GH-pituitary adenoma. Clinical neck examination showed an enlarged thyroid gland with a left paratracheal 1.6 x 1.2 cm solid nodule. Thyroidal function was normal [TSH: 3.6 μIU/ml (n.v.0.3-5.0); FT_3: 2.3 pg/ml (n.v. 1.8-3.4), FT_4:10.2 pg/ml (n.v.7.1-18.5)]. Nodule FNAB revealed a papillar thyroid carcinoma. Because of the multifocal localization of this neoplasia, we performed a total thyroidectomy and subsequent radiotherapy with ^{131}I on the small residual tumor because of the elevated neoplastic risk in a patient with elevated GH serum levels.
At the moment the patient is on L-Thyroxine suppressive therapy and the pituitary adenoma has been surgically removed.
This case emphasizes the well-known association between malignant tumors and acromegalic patients and it underlines the necessity for an accurate morfological thyroid examination and the importance of a citological examination of each nodule by FNAB.

LONG ACTING SOMATOSTATIN ANALOGUE LANREOTIDE, ASSOCIATED TO INTERFERON, IS NOT EFFECTIVE IN ADVANCED MEDULLARY THYROID CARCINOMA

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Treatment of advanced medullary thyroid carcinoma (MTC) is still very difficult. The possible benefits of microdissection for recurrent disease is questionable. Radiation therapy is reserved for skeletal metastases or non resectable metastatic MTC. Chemotherapy regimens have a limited, palliative role. Plasma calcitonin is the main marker in the follow up of this disease.
We evaluated the therapeutic effectiveness of lanreotide, a long acting somatostatin analogue associated to rIFN- α–2b in 4 patients with advanced, sporadic MTC (stage 3 or 4). Our patients received lanreotide 30 mg, i.m., two times a month and rIFN- α–2b, 3.000.000 UI, s.c., three times a week, for six months. CT and CEA plasma levels and morphologic staging by ultrasound, TC and MR, were evaluated at 0, 1, 3 and 6 months. No significative side effects were observed. Not significant decreases in CT and CEA levels nor changes in metastases size were observed during the treatment. These preliminary data don't seem to confirm a previous report about the effectiveness of somatostatin analogues (octreotide) and IFN on advanced CMT.

				CT pg/ml				CEA ng/ml			
Pts	Sex	Age	Stage	0	1	3	6	0	1	3	6
1	m	34	III	1540	997	2000	800	13	10	12	13
2	f	43	IV	1729	1296	1381	>2000	31	26	26	32
3	f	55	IV	1626	1492	869	1333	>70	>70	>70	>70
4	f	49	III	1140	1245	1233	1400	3,8	3.6	1,5	2.0

LONG-ACTING SOMATOSTATIN ANALOGUES ARE EFFECTIVE IN THE TREATMENT OF GRAVES' OPHTHALMOPATHY.

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The treatment of Graves' ophthalmopathy is still controversial: antinflammatory or immunomodulating drugs, radiotherapy and surgery are commonly used but their effectiveness is quite variable and also several side effects are usually encountered. Consequently their use is usually limited to patients with severe features and vision-threatening manifestations.
In this study we evaluated the effectiveness and tolerability of two long-acting somatostatin analogues, octreotide and lanreotide. The rationale of their use in Graves' ophthalmopathy is based on the detection of somatostatin receptors in retrobulbar tissues. It has been already hypothesized that their stimulation could reduce the inflammatory component of the ophthalmopathy.
We treated 5 patients (4 females and 1 male, 26-60 years old) with octreotide or lanreotide for a three month period. 2 patients received a 100 μg sc injection of octreotide three times a day, while 3 patients received a 30 mg im injection of lanreotide every 15 days. In 4 patients, before treatment, we investigated the presence of somatostatin receptors in the orbital area by [111In-DTPA-D-Phe1]octreotide scintigraphy. We compared clinical parameters, according to Werner NOSPECS classification, and sonographic findings, at the beginning and at the end of treatment. In all patients lid retraction and soft tissue involvement decreased. None of 2 patients with proptosis had a reduction of exophthalmos, while two out of 4 patients with extraocular muscle dysfunction showed an improvement of eye motion. In all patients orbital echography showed a decrease of medial rectus muscle thickness and retrobulbar tissue reflectivity. Treatment was well tolerated in all the cases.
In conclusion, somatostatin analogues, octreotide and lanreotide, seem to be an effective and safe treatment of Graves' ophthalmopathy. Their use is more efficacious on lid retraction and soft tissue involvement than on proptosis and eye motion and seems to be proposable in cases with a severe inflammatory component.

CMF + RADIOTHERAPY IN THE PRIMARY TREATMENT OF OPERABLE BREAST CANCER. PHASE II PILOT STUDY - PRELIMINARY RESULTS.

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Background and Objectives: Chemotherapy and radiotherapy have been investigated in several studies for their role in neoadjuvant treatment before surgery for breast cancer. We proposed a pilot study to evaluate a primary treatment scheme of alternate radiochemotherapy for operable (T2 - small T3) breast cancer.
Methods: Cyclophosphamide, methotrexate and 5-fluouracil (CMF) was administered on days 1 and 8 every four weeks, for two cycles. Radiotherapy was administered during the third and the fourth week, 5 days per week, after the beginning of chemotherapy. The patients were operated on within 2-4 weeks. All patients received four additional cycles of chemotherapy within one month after surgery.
Results: We observed one (8.3%) complete remission, 8 (66.7%) partial remissions, 3 (25%) stationery disease; no progressive disease was observed. Modified radical mastectomy was performed on 7 patients (58.3%). Conservative surgery was performed on 5 patients (41.7%). No major complications were observed. No patient had local or distant recurrence.

Conclusions : The feasibility is shown of primary chemoradiotherapy for breast cancer. To evaluate the impact of this therapy on overall survival and recurrence risk, and its possible introduction in clinical neoadjuvant breast cancer treatment, larger series and longer follow-up are needed.

PROGNOSTIC FACTORS IN DIFFERENTIATED THYROID CARCINOMA. A MULTIVARIATE ANALYSIS. Rocco Bellantone, Celestino Pio Lombardi, Mauro Boscherini, Angela Ferrante, Marco Raffaelli, Francesco Rubino, Maurizio Bossola, Francesco Crucitti, Istituto Clinica Chirurgica - Universita Cattolica Sacro Cuore, Roma, Italia.

Background and Objectives: Clinical characteristics and patient outcome of a group of patients treated for differentiated thyroid carcinoma were analyzed in order to assess the relative influence of different prognostic factors.

Materials and Methods: Data about sex, age, size and histologic behavior of the tumor, its extrathyroid extension, lymph node status, distant metastases at diagnosis, surgical procedures and overall survival from 234 patients, were retrospectively reviewed and subjected to statistical analysis.

Results: According to univariate analysis survival rates were significantly influenced by age (P=0.0001), size (P=0.018), extrathyroidal extension (P=0.000001), lymph node involvement (P=0.03), and distant metastasis (P=0.049). Age and size were independent at multivariate analysis (t=2.694 and t=2.443, respectively).

Conclusions: On the basis of these results and a review of the literature, we conclude that total thyroidectomy is the treatment of choice in differentiated thyroid carcinoma, except for small (less than 1 cm.) papillary carcinoma, that could be treated by lobectomy plus isthmectomy, while lymphadenectomy is indicated only in case of macroscopic involvement.